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REMARKS

Amendments to the Claims

Claim 1 has been amended to correct a typographical error. No other amendments to the claims have been made.

Claim Rejections - 35 USC § 103

Claims 1-12 and 15-17 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,042,849 to Richardson et al. ("Richardson" or "the `849 patent"), which discloses a pharmaceutical preparation containing ionic magnesium combined with additional therapeutic substances for the treatment and control of vasoconstriction and related conditions.

The Office Action states at page 3, lines 3-9 that:

> Richardson teaches an oral pharmaceutical composition comprising a dual layer combination tablet which is divided into two portions, one that is fully released into the stomach upon ingestion, and the other protected by an acid-resistant coating for release only in the intestine, whereby the intestine-release portion contains magnesium compounds/magnesium salts in combination with additional active agents and therapeutic substances, such as calcium and calcium salts (see reference column 6, line 62 through col. 11, line 55).

The dual layer combination tablet disclosed by Richardson combines calcium and magnesium so that they are simultaneously released into the body. Richardson does not disclose the sequential release of first calcium and then magnesium. The claims of the present invention specifically require the calcium component to be in the immediate release layer so that substantially all of the calcium is released before the delayed release magnesium

component begins to release in the intestine. This minimizes the effect of the calcium on the absorption of magnesium and provides more efficient magnesium absorption. The use of a time release component to limit the interaction of calcium with magnesium is neither taught nor suggested by Richardson.

Richardson teaches "a combination tablet in which the components are divided into two portions, one that is fully released into the stomach upon ingestion, and the other protected by an acid-resistant coating for release only in the intestine" (col. 9, lines 35-38). In discussing the dual layer combination tablet, Richardson does not disclose that calcium is included in either the first or second layer of the dual layer tablet (col. 9, lines 34-53 and Example 2). Richardson only teaches that Vitamin E can be in the first layer and that it immediately releases upon ingestion. However, Richardson does not teach a preference for calcium in either the immediate release layer or in the delayed release layer.

The combination of magnesium and calcium taught by Richardson is substantially different from the composition claimed in the present invention. Richardson teaches a "preparation [that] contains ionic magnesium combined with additional therapeutic substances in an interactive and complementary manner." Col. 3, lines 9-12. Richardson also teaches that "[a]dditional active agents are optionally included in the formulations" and that "[e]xamples [of the additional active agents] are calcium and calcium salts." Col. 7, lines 62-63 and 65. Thus, Richardson only teaches that calcium can be "included in the formulations" as an active agent (col. 7, lines 62-66) in combination with magnesium. There

is no teaching nor suggestion in Richardson that calcium can be in a layer of a dual layer tablet without being combined with magnesium.

Richardson does not teach a formulation or a two-layer tablet containing calcium and magnesium where the two components are <u>not</u> simultaneously released into the body. The time release layer of Richardson's dual layer tablet does not prevent calcium from interacting with magnesium. Moreover, the `849 patent does not teach the benefits of separating the calcium component from the magnesium component as required by the claims of the present invention. One of ordinary skill in the art would not find it obvious from the teachings of Richardson to form a dual layer tablet having calcium in the immediate release layer and magnesium in the delayed release layer.

The present invention teaches that calcium should not be combined with magnesium because it interacts with magnesium and decreases the absorption of magnesium by the body.

> The present invention is an orally administered pharmaceutical composition which provides controlled release of magnesium and includes a magnesium component, a controlled-release component and an interactive agent component. The interactive agent component [i.e., calcium] includes an agent which interacts with the host to affect bio-uptake of magnesium by the host. If the two components are released simultaneously in the gastrointestinal tract, the absorption of magnesium decreases. Therefore, the interactive agent component is released in the stomach and the release of the magnesium component is released in the intestine. The interactive agent dissolves in the gastric juice of the stomach and substantially all of the interactive agent is released before passage into the intestine of the host. The magnesium component includes magnesium or a magnesium compound and a release-controlling agent which substantially prevents release of magnesium until passage out of the stomach and into the intestine of the host.
>
> Specification, p. 7, lines 2-12.

Richardson merely teaches that a formulation can include both magnesium and calcium. However, Richardson does not teach that the interaction of calcium with magnesium prevents the efficient absorption of magnesium, nor does Richardson teach that formulations containing calcium and magnesium should include a means for limiting their interaction. Accordingly, the present invention is not obvious in view of the Richardson `849 patent.

Claims 13, 14 and 18 have been rejected under 35 U.S.C. 103(a) as being unpatentable over the `849 patent as applied to claims 1-12 and 15-17, and further in view of U.S. Patent No. 5,811,126 to Krishnamurthy et al. ("Krishnamurthy" or "the `126 patent") or U.S. Patent No. 4,339,428 to Tencza ("Tencza" or "the `428 patent"). The Office Action states (at page 5, line 17 to page 6, line 2) that Richardson discloses a formulation with a delay release of both magnesium and calcium in the intestine.

> Richardson, as discussed above, teaches an oral pharmaceutical composition comprising a dual layer combination tablet which is divided into two portions, one that is fully released into the stomach upon ingestion, and the other protected by an acid-resistant coating for release only in the intestine, whereby the intestine-release portion contains magnesium compounds/magnesium salts in combination with additional active agents and therapeutic substances, such as calcium and calcium salts.

Unlike Richardson, the composition of the present invention does not delay release both magnesium and calcium in the intestine. Instead, the claims of the present invention require a composition which immediately releases calcium in the stomach and delays the release of magnesium until it reaches the intestine. Richardson neither teaches nor suggests

releasing the calcium component separately from the magnesium component in order to limit the interference of calcium with the absorption of magnesium.

The Office Action states at page 6, lines 6-7 that "Krishnamurthy teaches a controlled release pharmaceutical composition for oral administration comprising a mixture of magnesium salt and calcium salt." Krishnamurthy teaches mixing calcium and magnesium together and does not teach nor suggest preventing them from interacting when released in the body. As discussed in more detail above with regard to Richardson, the claims of the present invention specifically require the separation of magnesium and calcium into two different components so that the calcium can be released immediately and the magnesium can be delay released after substantially all of the calcium has been released. Such a sequential release of the two components would not be possible if they were mixed together as Krishnamurthy teaches. Accordingly, Krishnamurthy, when combined with Richardson, does not make the present invention obvious since neither reference discloses a composition which releases calcium in the stomach and releases magnesium in the intestine in a manner that avoids substantial interaction between the two components.

The Office Action states at page 7, lines 3-5 that "Tencza teaches an oral pharmaceutical formulation comprising a combination of magnesium carbonate and calcium carbonate together with a magnesium oxide component." Tencza discloses a combination of calcium and magnesium which is similar to Richardson and Krishnamurthy, but quite different from the present invention. Tencza's combination fails to teach the composition of

the present invention which has separate and not combined calcium and magnesium components.

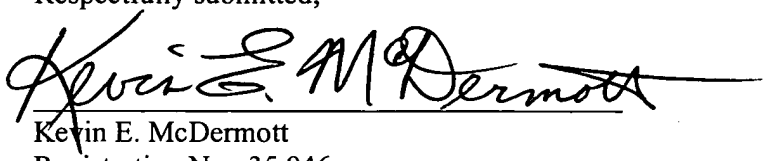
The formulations taught by Tencza do not have a delay release mechanism which prevents the calcium component and the magnesium component from releasing at the same time and interacting. Tencza does not address the problem caused by releasing calcium and magnesium at the same time and how it decreases the absorption of magnesium into the body. The present invention solves this problem by providing a two-component composition in which calcium is contained in the first component and releases immediately and magnesium is contained in the delay release component and does not release until it reaches the intestine. Tencza, when combined with Richardson, neither teaches nor suggests the sequential release of calcium in the stomach and magnesium in the intestine since both Tencza and Richardson teach formulations in which calcium and magnesium are mixed together and simultaneously released.

The applicants have found that a composition containing both calcium and magnesium is absorbed by the body most efficiently when the two components are released sequentially. Sequential release of calcium in the stomach and magnesium in the intestine decreases the interaction between the two components and prevents the calcium from significantly interfering with the absorption of magnesium.

Richardson, Krishnamurthy and Tencza, either alone or in combination, fail to disclose the sequential release of calcium and magnesium in order to avoid interaction between the two components. Moreover, there is no teaching or suggestion in any of these

references that would make the present invention obvious to one of ordinary skill in the art. Accordingly, the applicants respectfully request that the rejection of the claims as obvious in view of the cited art be withdrawn and that the claims be allowed.

Respectfully submitted,



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